Seasick Lungs

How Airborne Algal Toxins Trigger Asthma Symptoms

Adverse health effects from harmful algal blooms have most frequently been linked to eating fish or shellfish that have accumulated algal toxins. However, people have also suffered asthma-like symptoms after inhaling minute amounts of algal toxins that were aerosolized by waves. Now a research team uses an animal model to gain a better understanding of how exposure to airborne algal toxins causes these symptoms and whether available drugs can be used to prevent or relieve them [*EHP* **113:632–637**].

The researchers focused on toxins produced by a subtropical species of dinoflagellate (*Karenia brevis*) that is a major component of a bloom known as Florida red tide. *K. brevis* produces at least nine types of brevetoxins. When ingested, brevetoxins cause neurotoxic shellfish poisoning, with symptoms that can include numbness, tingling, and gastrointestinal distress. Persons exposed to aerosolized brevetoxins may suffer shortness of breath, sneezing, and other allergy- and asthma-like symptoms. Persons with preexisting airway disease appear most likely to be affected.

Waves of illness? Algal toxins from organisms such as *Karenia brevis* can be aerosolized in sea mist and breathed in by people. A mini-monograph in this issue examines the hazards they pose.

Dennis Kunkel Microscopy

To study airborne toxin exposure in a more controlled setting, the research team used a sheep model of asthma. The sheep model used is naturally sensitive to an antigen derived from the roundworm *Ascaris suum*, developing asthma-like symptoms (such as airway constriction) when exposed to this antigen. The sheep therefore can serve as surrogates for persons with asthma. To simulate environmental brevetoxin exposures, these allergic sheep were exposed to crude brevetoxins. These samples contained a variety of brevetoxin species (because multiple types are usually found in Florida red tide) as well as other parts of algal cells (because the toxin is usually released as the algae die and begin to decompose). In addition, the animals were also exposed to two types of purified brevetoxin, presumed to be the primary agent causing respiratory symptoms. In some studies the animals were treated before or after exposure with one of several clinically available medications.

Exposure to crude brevetoxins caused immediate bronchoconstriction in the sheep as evidenced by a twofold increase in airway constriction. This immediate bronchoconstriction was inhibited by 49% (compared with untreated animals) in animals that were pretreated with budesonide, by 71% in animals pretreated with albuterol, by 58% in animals pretreated with atropine, and by 47% in animals pretreated with diphenhydramine. In addition, bronchoconstriction was quickly reversed in animals that had not been premedicated if they were dosed with albuterol immediately after exposure.

The fact that diphenhydramine, a histamine antagonist, reduced airway symptoms indicates that brevetoxins activate histamine-producing cells, such as mast cells and basophils. Further proof of the involvement of these cells was gained from studies where toxin was injected into the animals' skin. In these skin tests, the reaction was up to 75% smaller if animals were pretreated with diphenhydramine.

The effectiveness of atropine, an anticholinergic agent, indicates that brevetoxins also activate neural pathways. The cholinergic pathway is involved in the regulation of the neurotransmitter acetylcholine, and is also activated by exposure to organophosphate pesticides.

The researchers also found that bronchoconstriction was reduced by 34% when animals were treated with HOE-140, a bradykinin β_2 receptor antagonist. This response indicates that, in addition to raising histamine levels, exposure to brevetoxins also increases the level of bradykinin, a protein with effects similar to histamine that has also been linked to asthma symptoms. Asthmatics are more sensitive to bradykinin than are individuals with normal airways, and kinin levels are increased in inflamed airways. This may explain why the researchers found that animals whose airways were already inflamed responded more strongly to brevetoxins. Thus, the increased responsiveness to toxin in persons with preexisting airway disease may be linked to their underlying airway inflammation at the time of toxin exposure.

This research shows that brevetoxins are potent airway constrictors, triggering several physiological pathways. The research has also determined drugs that could mitigate symptoms and serve as rescue medications for persons with severe reactions to brevetoxins. **–Kris Freeman**

Challenging Assumptions about Lead and IQ

Effects Increase, Not Decrease, in Older Children

The concentration of lead in children's blood peaks at about age 2 years and then declines as hand-to-mouth activity tends to drop off. Much of the practice and research concerning lead poisoning is based on the belief that the most damage is done by that peak. However, lead's effects on IQ cannot be detected until about 4 or 5 years of age, when IQ becomes testable. Thus, researchers assume, if we wish to know the lowest level at which lead causes damage, we have to measure blood lead in 2-year-olds and follow them, and if we wish to prevent lead toxicity from occurring, we should focus on 2-year-olds. Both assumptions, and the outcomes they encourage, may be incorrect, concludes a U.S. research team after analyzing data from a study that began in 1994 [*EHP* **113:597–601**].

The Treatment of Lead-Exposed Children study was initially designed to evaluate whether a drug called succimer, which lowers blood lead, would reduce or prevent the effects of lead on IQ. The 780 participating children, selected in approximately equal numbers from clinical centers in Baltimore, Cincinnati, Newark, and Philadelphia, were regularly tested for blood lead concentration and given IQ tests from about age 2 years to about age 7.5 years. About half the children had taken succimer, while the others had taken a placebo. The drug lowered the children's blood lead concentrations, but the group given succimer did no better on IQ tests than the group given placebo.

In the current study, researchers used the earlier data to evaluate the strength of the association between IQ and blood lead at various ages, and whether blood lead at age 2 years affected IQ at ages 5 and 7 more than blood lead measured at the older ages. The team examined blood lead and intelligence data from ages 2, 5, and 7, as well as many other factors, such as race, sex, language spoken, caregiver's IQ, and parent's education, employment, and status as a single parent.

Contrary to most current thinking, which assumes that blood lead concentration at age 2 is the best predictor of IQ at ages 5 and 7, this team found that concurrent blood lead concentration had the strongest association with IQ, and the older the child, the stronger the association. This was true even though blood lead concentrations dropped progressively as the children aged. A few other studies had found somewhat similar results, but the researchers say the size of this study and the quality of its data reinforce the strength of the findings.

This study does have some drawbacks. For instance, the investigators had no data reflecting how much caregivers interacted with and stimulated the children, which can influence a child's intelligence. In addition, the children selected for the original study weren't representative of the population as a whole. For instance, their initial blood lead concentrations were higher than those of most U.S. children today, 77% of the children were black, 97% were receiving public assistance, and 72% lived in single-parent households.

Nonetheless, the team concludes that ongoing lead contamination has a significant effect on a child's intelligence, emphasizing the importance of testing for and reducing lead contamination in the environment of children much older than typically targeted. They also say the findings, if they hold up and are accepted, would relax an important limitation on lead studies, allowing future efforts to include subjects who were not tested for lead at age 2. **–Bob Weinhold**

Poultry's Persistence Problem

Drug-Resistant *Campylobacter* in Chicken

Mounting evidence suggests that the poultry industry's use of antibiotics promotes antibiotic resistance among the foodborne bacteria that infect humans. One such bacterium is *Campylobacter*, a pathogen common to chicken products. Every year more than 1 million Americans develop *Campylobacter*-induced food poisoning from eating undercooked contaminated chicken. Resistant strains of *Campylobacter* are a growing public health threat, particularly among elderly and immunocompromised patients. This month, researchers from the Johns Hopkins Bloomberg School of Public Health provide evidence suggesting that chickens raised without antibiotics are less likely to carry antibiotic-resistant strains of *Campylobacter* [*EHP* 113:557–560].

The study focused on fluoroquinolones (FQs), a class of antimicrobials used to control the bacterium *Escherichia coli* in broiler chickens. Of the two FQs initially approved for use in poultry, Sara Flox WSP and Baytril, only the latter remains on the market. The Food and Drug Administration is seeking to repeal approval for Baytril due to concerns that it contributes to microbial resistance.

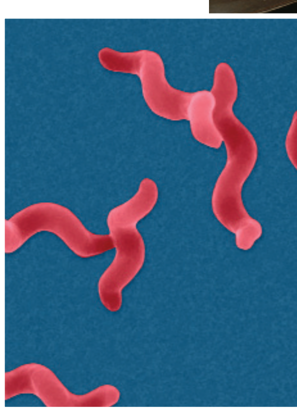
The authors collected chicken products from two "antibiotic-free" producers (Bell & Evans and Eberly Poultry) and two of the nation's largest conventional producers (Tyson Foods and Perdue Farms). The conventional producers claimed to have stopped using FQs in February 2002. The authors began sampling chicken products one year later, in 2003. All samples were obtained from grocery stores in or near Baltimore, Maryland.

Chicken samples were processed using standard isolation techniques; however, at the final step, *Campylobacter* enrichments were streaked onto agar plates both with and without ciprofloxacin (a second-generation FQ used to treat human disease). The ciprofloxacin supplement enabled the authors to identify FQ-resistant *Campylobacter* isolates from among a mix of susceptible and resistant strains.

Campylobacter was detected on 84% of all the samples tested. FQ-resistant strains were detected on 17% using unsupplemented agar and on 40% using supplemented agar. Abstention from FQ use by poultry producers did not increase the likelihood of *Campylobacter* contamination. Moreover, conventional products were up to 460 times more likely to carry resistant strains than their antibiotic-free counterparts. Of particular interest is that FQ resistance in conventional products persisted for one year after cessation of industrial use.

Based on these findings, the authors suggest that even without antibiotics, resistant populations may remain prevalent over time. Persistence of these resistant populations may result from residual contamination in poultry houses, the authors suggest. For example, biofilms in water distribution systems can harbor *Campylobacter* and thus could serve as reservoirs for resistant populations. These findings suggest the need to further improve poultry house cleaning and disinfection, they write.

The authors say it is important to measure the prevalence of, and causes for, FQ-resistant strains in the food supply. To this end, they point out that supplemented agar may provide a much more sensitive tool than conventional methods for detecting resistant strains of the bacterium. **–Charles W. Schmidt**



Photodisc; inset: Dennis Kunkel Microscopy

Chicken surprise. New data show that antibiotic-resistant *Campylobacter* (left) can persist in poultry populations—and products—long after producers stop using the drugs.